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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,192	12/20/2006	Sanjay Kumar Vaishnav	U 016181-4	1783
140	7590	07/02/2008		
LADAS & PARRY LLP 26 WEST 61ST STREET NEW YORK, NY 10023			EXAMINER CHANDRAKUMAR, NIZAL S	
			ART UNIT	PAPER NUMBER
			1625	
			MAIL DATE	DELIVERY MODE
			07/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/571,192	Applicant(s) VAISHNAV ET AL.	
	Examiner NIZAL S. CHANDRAKUMAR	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/09/2006</u> . | 6) <input type="checkbox"/> Other: ____. |

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

DETAILED ACTION

This application filed 12/20/2006 is a 371 of PCT/IN03/00333 10/14/2003.

Claims 1-14 are before the Examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim language 'adjusting the pH of fermentation broth containing mevinolinic acid at 3.5 = or - 0.1 with miner acid' is vague because it is unclear if acid was added to the broth to adjust the pH at 3.5 = or - 0.1, or if acid is added to broth which is already at pH at 3.5 = or - 0.1. Likewise, step C), line 1, the use of the term 'at' is unclear.

The structure of mevinolinic acid is pictured after step d) and the number (II) is not associated with the structure.

In step C) line 3, it is unclear what 'f' means.

The claims are also drawn to terms 'pure' , 'extra pure' that are unclear because it is unclear what level of purity is considered impure, pure, or extrapure etc..

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1625

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al. US 7052886.

Instant claims

The claims of the instant case are drawn to a process of making Lovastatin from fermentation broth containing mevilonic acid. Shown below, is the method of the instant case

Lovastatin broth [4500gms; containing (34.2) gms of mevilonic acid (II)] was added into a flask and cooled to 20°C, and the pH was adjusted to 3.5 ± 0.1 by addition of 85% orthophosphoric acid (60gms). Toluene (11250ml) was added and the mixture agitated to 55 ± 5°C for 19.0 hours in a nitrogen atmosphere. The organic layer was separated and washed twice with 2.5% aqueous sodium bicarbonate solution (580 ml). The organic layer was washed with water (580ml) and the organic layer concentrated under vacuum at 35-40°C. Toluene (260ml) was added to the residue and the mixture was cooled to -5 °C for complete crystallization of Lovastatin (I) in a period of 4.0 hours. The mixture was filtered and the wet cake washed with chilled toluene (50ml). The wet cake was dried at 35-40°C to give impure Lovastatin (I) 26.6gm; %Yield 76.12; %purity 93.7.

Prior art

Kumar et al. teach a process for the preparation and isolation of Lovastatin from fermentation broth containing mevilonic acid. Reaction parameters such as acidification, duration of time of reaction,

filtration, temperature, extraction solvent etc of Kumar et al. as shown below are not substantially different from those of the instant claims.

To 6.2 L of fermentation broth, 0.80 L of dilute sulfuric acid (2N) was added to bring the pH to 2.1. The acidified broth was heated to about 50° C. and was stirred at 50–60° C. for about 24 hours. 90% of the acid form was converted to lactone form as monitored by High Pressure Liquid Chromatography.

The broth was filtered and the mycelial cake was extracted with 7.5 L of toluene. The toluene extract was washed with 1.3 L of 5% w/v sodium bicarbonate solution and 0.65 L of demineralised water. The washed toluene extract was concentrated under vacuum at about 60° C., to a volume of about 160–200 mL. The concentrate was cooled to 5–7° C. and stirred further for 1 hour. The slurry was then filtered and the cake was washed with 50 mL of pre-cooled (5–10° C.) toluene. The wet cake was dried at 40° C. under vacuum for 16 hours. 25.6 g of Lovastatin with a chromatographic purity of more than 95% was obtained.

To 12 L of fermentation broth, 1.40 L of dilute nitric acid (10%) was added to bring the pH to 2.2. The acidified broth was heated to about 50° C. and was stirred at this temperature for about 48 hours. 90% of the acid form was converted to lactone form as monitored by High Pressure Liquid Chromatography.

The broth was filtered and the mycelial cake was extracted with 12 L of toluene. The toluene extract was washed with 1.5 L of 5% w/v sodium bicarbonate solution and 1.5 L of demineralised water. The washed toluene extract was concentrated under vacuum at about 50° C., to a volume of about 300–350 mL. The concentrate was cooled to 5–7° C. and stirred at this temperature for 3 hours. The slurry was then filtered and the cake was washed with 100 mL of pre-cooled (5–10° C.) toluene. The wet cake was dried at 40° C. under vacuum. 46.2 g of Lovastatin with a chromatographic purity of more than 95% was obtained.

Kumar et al. do not teach all the particulars of the instant process, that is the instant claim limitations, such as temperature, that are identical to the ones employed in the instant case.

Motivation:

One skilled in the art of organic process research in pursuit of alternate processes for making commercially important Lovastatin, would be motivated to use, as matter of routine experimentation in optimization of cost and efficiency to find alternate reaction parameters such as reagents, solvents, temperature etc with reasonable expectation of success because, of the teachings of Kumar et al. For example, the temperature for precipitation/crystallization 5–7° C of Kumar et. al. is not different from –5° C of the instant case. The essential and critical steps necessary for the production of Lovastatin are same in the prior art process and the instantly claimed process. Likewise, the application of crystallization and solid support such as alumina for purification purposes are well within the skill one of ordinary skill in the organic chemistry art.

Thus it would have been obvious to one of ordinary skill in the art to modify an otherwise known process to obtain known product using analogous reagents and alternate conditions in lieu of another as the results would not have been unexpected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nizal S. Chandrakumar

/D. Margaret Seaman/
Primary Examiner, Art Unit 1625